



## U.S. Environmental Protection Agency Integrated Risk Information System

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### Acetophenone (CASRN 98-86-2)

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#### Acetophenone; CASRN 98-86-2

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

#### STATUS OF DATA FOR Acetophenone

File First On-Line 08/22/1988

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	01/01/1989
Inhalation RfC Assessment (I.B.)	no data	08/01/1992
Carcinogenicity Assessment (II.)	on-line	02/01/1991

#### I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

##### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name -- Acetophenone  
CASRN -- 98-86-2  
Last Revised -- 01/01/1989

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other

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sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

#### I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
General toxicity	NOAEL: 10,000 ppm (423 mg/kg/day)	3000	1	1E-1 mg/kg bw/day
Rat Oral Subchronic Study	LOAEL: None			
Hagen et al., 1967				

\* Conversion Factors: Investigators determined that 15.5% volatilized, thus 10,000 ppm x 0.845 = 8450 ppm. Assuming a rat consumes a daily amount of food equal to 5% of its body weight, 8450 ppm (mg/kg food) x 0.05 kg food/kg bw = 423 mg/kg/day.

#### I.A.2. Principal and Supporting Studies (Oral RfD)

Hagan, E.C., W.H. Hansen, O.G. Fitzhugh, et al. 1967. Food flavorings and compounds of related structure. II. Subacute and chronic toxicity. Food Cosmet. Toxicol. 5: 141-157.

No effects on growth, hematological values or macroscopic tissue changes were observed in groups of 10 male and 10 female Osborne-Mendel rats exposed to 0, 1000, 2500 and 10,000 ppm acetophenone in the diet for 17 weeks. Microscopic examination of the 10,000 ppm group revealed no effects. Thus, the 10,000 ppm level was the highest concentration at which no effects were observed. Some loss of the compound from the feed due to volatilization was reported; therefore, the dietary concentration of 10,000 ppm was multiplied by a factor of 0.845 (based on data provided by the investigators) yielding a NOAEL of 8450 ppm or 423 mg/kg/day assuming that a rat consumes a daily amount of food equivalent to 5% of its body weight/day as food. Dividing the dose by an uncertainty factor of 3000 yields the RfD of 0.4 mg/kg/day or 7 mg/day for a 70 kg person.

#### I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF – 10 for species to species extrapolation, 10 to protect sensitive humans, 10 to extrapolate from subchronic to chronic exposure, and 3 for the lack of important reproductive toxicity data.

MF – None

#### I.A.4. Additional Studies/Comments (Oral RfD)

Single dose oral LD50 values for rats range from 0.9-3.2 g/kg bw indicating that the subchronic NOAEL defined by Hagan et al. (1967) may be close to the threshold for toxicity.

Acetophenone has not been tested for carcinogenicity teratogenicity or for reproductive effects.

#### I.A.5. Confidence in the Oral RfD

[Quantitative Estimate of Carcinogenic Risk from Oral Exposure](#)

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[Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure](#)

[- Summary of Risk Estimates](#)  
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Study – Low  
Database -- Low  
RfD – Low

The study was given a low confidence level because although the animals were tested by a relevant route of administration at three levels in a subchronic study and several endpoints were monitored, the sample size was inadequate and the range of doses tested did not define a LOAEL. The database was given a low confidence level because although NOAELs were defined by Hagan et al. (1967), supporting studies could not be located in the available literature. In addition, only one species was tested, and no carcinogenicity, teratogenicity or reproductive studies could be located in the available literature. Further, the only supporting data available was acute toxicity data, which indicated that the NOAEL defined by Hagan et al. (1967) was close to the threshold of toxicity. Thus, the RfD was given a low confidence level rating.

#### I.A.6. EPA Documentation and Review of the Oral RfD

Source Document -- This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation -- None

Agency Work Group Review -- 10/15/1987

Verification Date -- 10/15/1987

Screening-Level Literature Review Findings -- A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for acetophenone conducted in August 2003 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or 202-566-1676.

#### I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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#### I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name -- Acetophenone  
CASRN -- 98-86-2

Not available at this time.

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#### II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name -- Acetophenone  
CASRN -- 98-86-2  
Last Revised -- 02/01/1991

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

## **II.A. Evidence for Human Carcinogenicity**

### **II.A.1. Weight-of-Evidence Characterization**

Classification -- D; not classifiable as to human carcinogenicity

Basis -- Based on no human data and no animal data.

### **II.A.2. Human Carcinogenicity Data**

None.

### **II.A.3. Animal Carcinogenicity Data**

None.

### **II.A.4. Supporting Data for Carcinogenicity**

In a plate incorporation assay at levels of up to 3000 nmol/plate acetophenone was not mutagenic when tested for reverse mutations in several strains of *Salmonella typhimurium* both in the presence and absence of rat S-9 hepatic homogenates (Elliger et al., 1984). Rahn et al. (1974) found that acetophenone caused breaks in DNA isolated from *E. coli* (B(3)T-) after strand photosensitization.

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## **II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure**

None.

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**\_II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure**

None

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**\_II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)**

**\_\_II.D.1. EPA Documentation**

Source Document – U.S. EPA, 1987

The 1987 Health and Environmental Effects Document for Acetophenone has received peer review and Agency review and is approved for publication.

**\_\_II.D.2. EPA Review (Carcinogenicity Assessment)**

Agency Work Group Review – 11/07/1990

Verification Date – 11/07/1990

Screening-Level Literature Review Findings – A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for acetophenone conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or 202-566-1676.

**\_\_II.D.3. EPA Contacts (Carcinogenicity Assessment)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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**\_III. [reserved]**

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**\_V. [reserved]**

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**\_VI. Bibliography**

Substance Name – Acetophenone  
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Last Revised – 02/01/1991

**\_VI.A. Oral RfD References**

Hagan, E.C., W.H. Hansen, O.G. Fitzhugh, et al. 1967. Food flavorings and compounds of related structure. II. Subacute and chronic toxicity. Food Cosmet. Toxicol. 5: 141-157.

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#### **\_VI.B. Inhalation RfC References**

None

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#### **\_VI.C. Carcinogenicity Assessment References**

Elliger, C.A., P.R. Henika and J.T. MacGregor. 1984. Mutagenicity of flavones, chromones and acetophenones in *Salmonella typhimurium*: New structure-activity relationships. Mutat. Res. 135: 77-86.

Rahn, R.O., L.C. Landry and W.L. Carrier. 1974. Formation of chain breaks and thymine dimers in DNA upon photosensitization at 313 nm with acetophenone, acetone or benzophenone. Photochem. Photobiol. 19(1): 75-78.

U.S. EPA. 1987. Health and Environmental Effects Document for Acetophenone. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

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#### **\_VII. Revision History**

Substance Name – Acetophenone  
CASRN – 98-86-2

Date	Section	Description
08/22/1988	I.A.	Oral RfD summary on-line
01/01/1989	I.A.7.	Contacts phone numbers corrected
08/01/1989	VI.	Bibliography on-line
12/01/1990	II.	Carcinogen assessment now under review
02/01/1991	II.	Carcinogenicity assessment on-line
02/01/1991	VI.C.	Carcinogen references added
09/01/1991	I.B.	Inhalation RfC now under review
01/01/1992	I.A.7.	Secondary contact changed
01/01/1992	IV.	Regulatory Action section on-line
08/01/1992	I.B.	Work group review meeting date added
08/01/1995	I.B.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical

substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the workgroup functions beginning in September, 1995.

04/01/1997 III., IV., V.

Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

10/28/2003 I.A.6.,  
II.D.2.

Screening-Level Literature Review Findings message has been added.

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## **\_VIII. Synonyms**

Substance Name -- Acetophenone  
CASRN -- 98-86-2  
Last Revised -- 08/22/1988

98-86-2  
Acetophenone  
acetyl benzene  
hypnone  
phenyl methyl acetone

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Last updated on Thursday, November 18th, 2004  
URL: <http://www.epa.gov/iris/subst/0321.htm>